Listing of the Claims:

1. (previously presented) A polynucleotide comprising a non-naturally occurring HCV sequence that is capable of productive replication in a host cell, or is capable of being transcribed into a non-naturally occurring HCV sequence that is capable of productive replication in a host cell, wherein the HCV sequence comprises, from 5' to 3' on the positive-sense nucleic acid, a functional 5' non-translated region (5' NTR); one or more protein coding regions, including at least one polyprotein coding region that is capable of replicating HCV RNA; and a functional HCV 3' non-translated region (3' NTR), wherein said polynucleotide further comprises an adaptive mutation in the NS5A coding region that confers improved cell culture characteristics to said polynucleotide.

2. (canceled)

3. (previously presented) The polynucleotide of claim 1, having a transfection efficiency into mammalian cells of greater than 0.01%.

4. (original) The polynucleotide of claim 3, wherein the transfection efficiency into mammalian cells is greater than 0.1%.

5. (original) The polynucleotide of claim 3, wherein the transfection efficiency into mammalian cells is greater than 1%.

6. (original) The polynucleotide of claim 3, wherein the transfection efficiency into mammalian cells is greater than 5%.

7. (previously presented) The polynucleotide of claim 1, wherein the polynucleotide is capable of replication in a non-hepatic cell.

8. (original) The polynucleotide of claim 7, wherein the non-hepatic cell is a HeLa cell.

9. (previously presented)The polynucleotide of claim 1, wherein the HCV is impaired in its ability to cause disease, establish chronic infections, trigger autoimmune responses, and transform cells.

10-11. (canceled)

12. (previously presented) The polynucleotide of claim 1, wherein the mutation is within 50 nucleotides of an interferon sensitivity determining region (ISDR) or includes the ISDR.

13. (original) The polynucleotide of claim 12, wherein the mutation is within 20 nt of the ISDR, or includes the ISDR.

14. (original) The polynucleotide of claim 13, wherein the mutation encodes an amino acid sequence change selected from the group consisting of Ser (1179) to Ile, Arg (1164) to Gly, Ala(1174) to Ser, Ser(1172) to Cys, and Ser(1172) to Pro of SEQ ID NO:3.

15. (original) The polynucleotide of claim 11, wherein the mutation comprises a deletion of at least a portion of the ISDR.

16. (original) The polynucleotide of claim 15, wherein the mutation comprises a deletion of the entire ISDR.

17. (original) The polynucleotide of claim 16, wherein the mutation comprises a deletion of nucleotides corresponding to nucleotides 5345 to 5485 of SEQ ID NO:6.

18-28. (canceled)

29. (currently amended) The polynucleotide of claim 1, wherein the transfection efficiency into mammalian cells is about 6%.

30-60. (canceled)

61. (original) The polynucleotide of claim 1, wherein the polynucleotide is double-stranded DNA.

62. (original) A vector comprising the polynucleotide of claim 61 operably associated with a promoter.

63-68. (canceled)

69. (original) A cell comprising the vector of claim 62.

70. (previously presented) A host cell comprising the polynucleotide of claim 1, wherein the host cell is a mammalian cell.

71. (canceled)

72. (previously presented) The host cell of claim 70 wherein the host cell is a human cell.

73. (original) The host cell of claim 72 wherein the host cell is a liver cell.

74-85. (canceled)

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~~87.~~ 86 (previously presented) The polynucleotide of claim 1, further comprising a mutation in the NS3 or NS4B coding region.